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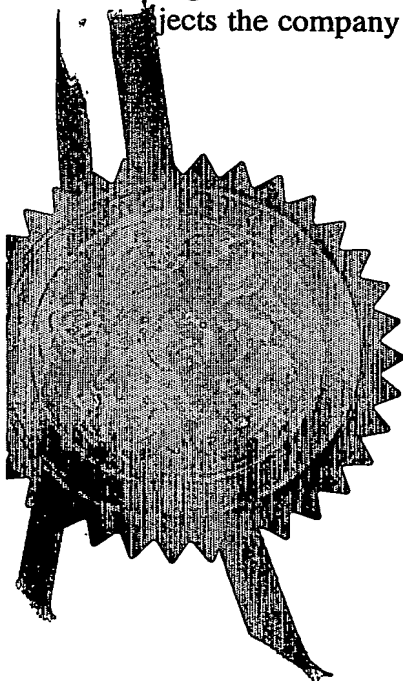
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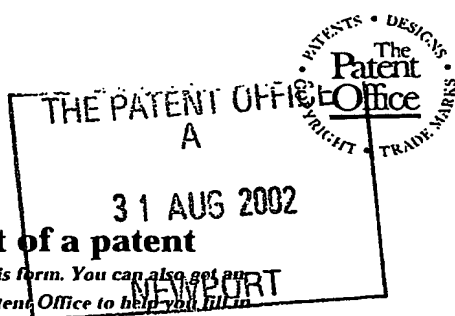
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P01/7700 0.00-0220312.3

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(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

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1. Your reference **srt.1886.uk.cr.d**

2. Patent application number
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31 AUG 2002

0220312.3

3. Full name, address and postcode of the or of each applicant (underline all surnames)

Professor Neil Graham
6 Kilmardinny Grove
Bearsden
GLASGOW
G61 3NY

08456410001

Patents ADP number (if you know it)

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention

Novel thermoplastic hydrogel polymer compositions for use in producing contact lenses and methods of producing said compositions

5. Name of your agent (if you have one)

Kennedys Patent Agency Limited

"Address for service" in the United Kingdom to which all correspondence should be sent (including the postcode)

Floor 5, Queens House
29 St Vincent Place
GLASGOW
G1 2DT

Patents ADP number (if you know it)

08058240002

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number

Country

Priority application number
(if you know it)

Date of filing
(day / month / year)

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application

Date of filing
(day / month / year)

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? (Answer 'Yes' if:

No

- a) any applicant named in part 3 is not an inventor; or
 - b) there is an inventor who is not named as an applicant; or
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Patents Form 1/77

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Continuation sheets of this form

Description 11

Claim(s)

Abstract

Drawing(s) 1 + 1

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Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (*Patents Form 7/77*)

Request for preliminary examination and search (*Patents Form 9/77*)

Request for substantive examination (*Patents Form 10/77*)

Any other documents
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11. I/We request the grant of a patent on the basis of this application.

Kennedys

Signature
KENNEDYS

Date
30 August 2002

12. Name and daytime telephone number of person to contact in the United Kingdom
- | | |
|-------------------|---------------|
| Claire Rutherford | 0141 226 6826 |
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1 Novel Thermoplastic Hydrogel Polymer Compositions for use
2 in producing contact lenses and Methods of Producing said
3 Compositions

4
5 The present invention relates generally to production of
6 thermoplastic hydrogels for use as contact lenses. In
7 particular, the invention relates to thermoplastic
8 hydrogels which show improved flow characteristics.

9
10 It is already known in the art to make contact lenses
11 using hydrogels. Generally these hydrogels are HEMA, NVP
12 or products of free radical polymerisation. However,
13 these compositions generally do not flow and can only be
14 moulded by reaction injection moulding (RIM), which is a
15 slow and relatively expensive process which is not
16 particularly suited to contact lens manufacture.

17
18 Also, existing reaction injection moulding techniques
19 utilise free radical initiation or irradiation cure that
20 produces radicals. These radicals initiate a
21 peroxidation chain process, which leads ultimately to
22 damage of PEO based polymers in storage for use which
23 gives a short life to contact lenses produced from them.

1 There are also problems with bio-compatibility of
2 reaction injection moulded hydrogels which again is not
3 ideal for the manufacture of contact lenses where bio-
4 compatibility is importantant.

5
6 Additionally, the current cross linked polymer hydrogels
7 often have a very poor resistance to crack initiation and
8 crack propagation which again can be problematic when
9 producing contact lenses.

10
11 It can therefore be seen that it would be beneficial to
12 provide thermoplastic hydrogels which are capable of
13 being generally moulded under pressure so that contact
14 lenses can be easily and cheaply produced.

15
16 It is an aim of the present invention to provide a
17 thermoplastic hydrogel composition which has the ability
18 to flow under moderate shear at particular temperatures
19 below the polymer decomposition temperature.

20
21 It is a further object of the present invention to
22 provide a thermoplastic hydrogel composition which can be
23 injection or compression moulded.

24
25 It is a further object of the present invention to
26 provide a solvent soluble composition.

27
28 Another object of the present invention is to provide a
29 thermoplastic hydrogel composition which is highly bio
30 compatible.

31
32 A yet further object of the present invention is to
33 provide thermoplastic hydrogels which have a high level

1 of water swelling properties after moulding and swelling
2 with water.

3

4 According to a first aspect of the present invention,
5 there is provided a method of producing thermoplastic
6 hydrogels for use in producing contact lenses, comprising
7 the steps of reacting one or more from the list;

8 polyethylene oxide,

9 polyol,

10 polyamine,

11 with a polyisocyanate and a polyfunctional amine or
12 alcohol.

13

14 Preferably the polyol is polyethylene glycol.

15

16 Preferably, the method also comprises the step of end
17 capping unreacted groups with a unit capable of producing
18 hydrogen bonding, π bonding, ionic bonding and/or phase
19 separation or forming a glassy phase separated domain.

20

21 Alternatively, according to a second aspect of the
22 present invention, the method also comprises the step of
23 end capping unreacted groups with a unit from a list of:

24 Mono-functional amine

25 Mono-functional isocyanate

26 Monofunctional anhydride

27 Acid

28 Mono-functional hydroxyl

29

30 Preferably the reaction between one or more from the list

31 polyethylene oxide

32 polyol

33 polyamine

1 and a polyisocyanate is prepared using a range of NCO:OH
2 or NCO:NH₂ ratios.

3
4 Optionally a biodegradable unit may be incorporated.

5
6 The biodegradable unit may be polycaprolactone, poly
7 (lactic acid), poly(glycolic) acid or
8 poly(hydroxybutyric)acid, amine or hydroxyl ended
9 poly(amino) acids (protein or peptide analogues).

10
11 The ratios are preferably selected such that, at complete
12 reaction, the product does not form a macrogel.

13
14 Preferably the first step reaction is prepared using a
15 range of NCO:OH OH or NCO:NH₂ ratios from 2:1 to 1:2.

16
17 Most preferably the first step reaction is prepared using
18 NCO:OH OH or NCO:NH₂ ratios of 2.0:1 to 1:1.8 and 1.8:1 to
19 1:1.8.

20
21 Optionally the range of ratios used may be extended by
22 the addition of monofunctional amines, alcohols or
23 cyanates.

24
25 Alternatively, a macrogel is prevented from forming by
26 stopping the reaction before completion.

27
28 Preferably, the reaction is stopped by the addition of a
29 monoamine or an amine terminated polymer.

30
31 Optionally, the monoamine or an amine terminated polymer
32 is added when the reaction is partially complete.

33

1 Alternatively, an amine is admixed at the outset thus
2 removing the possibility of gelation.

3
4 Preferably, the amine is added in the form of amine
5 carbonate.

6
7 Typically, products with NCO end groups are subjected to
8 a final curing by immersion in liquid water or steam
9 after moulding.

10
11 Preferably, in the second stage the unreacted groups are
12 capped with an amine.

13
14 Optionally, unreacted NCO groups are endcapped.

15
16 Another option is that unreacted OH groups are endcapped.

17
18 Preferably, terminal NCO groups are converted into a
19 strongly hydrogen bonding urea group.

20
21 Preferably, the unreacted groups are capped with an
22 aliphatic amine.

23
24 Optionally, the amine group is attached to a long linear
25 or branched alkyl group or to an aryl- or aralkyl-amine.

26
27 Optionally, the amine group is attached to polymers or
28 low molecular weight pre-polymers.

29
30 Alternatively, excess OH groups are capped with one or
31 more molecules from the list of;

32 mono-isocyanate ended aromatic molecules,
33 mono-acid anhydride ended aromatic molecules,

1 mono-isocyanate ended aliphatic molecules,
2 mono-acid anhydride ended aliphatic molecules
3 reaction product of a monoamine with a di(or higher)
4 isocyanate.

5
6 The groups used in the endcapping process allow the
7 polymers to interact with physical or chemical cross-
8 linking. The separate particles therefore bind to each
9 other.

10
11 According to the third aspect of this invention there is
12 provided a thermoplastic hydrogel for use in producing
13 contact lenses produced by the methods of the first and
14 second aspects.

15
16 Preferably, the hydrogel is completely polymerised under
17 the specific conditions that are being used.

18
19 Preferably, after polymerisation the hydrogel is heated.

20
21 Alternatively, after polymerisation the hydrogel is
22 immersed in water liquid or vapour.

23
24 Optionally, the end product may be pelletised, pressed,
25 extruded or heat, pressure, injection or compression
26 moulded.

27
28 Preferably, the end product incorporates an antioxidant
29 containing two or more hydroxyl groups.

30
31 The antioxidant may be internal or external.

32
33 Preferably, the antioxidant is ascorbic acid.

1
2 Alternatively, the antioxidant is 2,6-ditertiarybutyl4-
3 hydroxanisol.

4
5 Optionally, the end product can incorporate dye.

6
7 According to a fourth aspect of the present invention
8 there is provided a contact lens produced from the
9 hydrogel of the third aspect.

10
11 An example of the present invention will now be
12 illustrated by way of example only and with reference to
13 the following figure, in which:

14
15 Figure 1 shows typical end groups that could be envisaged
16 as being associated in stacks as shown.

17
18 In the preferred embodiment, the thermoplastic materials
19 are prepared from mixtures of di (or higher) PEG polyol
20 with a di (or higher) polyisocyanate and/or a di (or
21 higher) polyamine.

22
23 First stage materials can also be made from many step-
24 growth reactions amongst which the reaction of PEG
25 polyols with polyacids with removal of reactive-produced
26 water is an option. The production of first stage
27 materials can also be guided by the art of making alkid
28 resins in the paint industry.

29
30 If the product from the first stage reaction is made from
31 a mixture of PEG diol, 1, 2, 6-hexantriol and
32 diphenylmethane-4,4-diisocyanate, it can be prepared
33 using a range of NCO:OH ratios from, for example, 2:1 to

1 1:2. At the extremes of these ratios, the 2:1 will have
2 all NCO unreacted groups and the 1:2 ratio will have all
3 OH unreacted groups. These compositions are not able to
4 macrogel and will contain only small proportions of low
5 molecular rate branched polymers. The product is a fluid
6 and suitable for injection, extrusion or compression
7 moulding at temperatures which are typically below 150°C,
8 although temperatures of 200°C to 250°C can be utilised
9 for short periods. It should be noted that the products
10 with NCO end groups can only be moulded and subjected to
11 final curing by immersion in liquid water or steam for a
12 suitable period.

13
14 It is possible to use intermediate NCO:OH ratios, such as
15 2:1 to 1:1.8 and 1.8:1 to 1:1.8 (and these ranges can be
16 further extended by the addition of mono-functional
17 molecules). As these still provide at complete reaction,
18 fluid systems, which when the end groups, are NCO can be
19 injection moulded and post-cured by water or steam
20 immersion. However, depending on the proportion of tri
21 or higher functional materials, ratios such as 1.6:1 to
22 1:1.6 form macrogels at as complete a reaction as is
23 possible with the NCO and OH groups present (and less
24 extended ratios are possible if mono-functional amines,
25 alcohols or cyanates are used in the first stage. The
26 resulting products are not fuseable and are not solvent
27 soluble). It is possible that the products may still be
28 used for the second stage of the process, to give useful
29 end capped products, if the reaction is stopped before it
30 has proceeded as far as possible. This operation is less
31 convenient and more difficult as the degree of completion
32 of the reaction must be determined using, for example,
33 infra-red analysis of the isocyanate absorption peak of

1 the reaction mixture, or by the viscosity of the
2 reaction. Therefore, it is much preferred to use the
3 compositions which cannot macrogel, as they can be taken
4 to completion of the first stage without fear of
5 irreversibly solidifying the reactants.

6
7 A preferred embodiment is that the first stage product is
8 a heavily branched polyurethane/PEG resin. In this
9 embodiment, the second stage is intended to convert each
10 of the terminal groups into a strongly hydrogen bonding
11 urea group. An aliphatic amine could be used and the
12 amine group could be attached to a short or long linear
13 or branched (preferably linear) alkyl group, such as
14 decyl or stearic or higher polyamines such as
15 polyethylene, or to an aryl or aralkylamine, such as
16 aniline, aminoanthracene or octylaniline. The
17 combination of the urea group and the long aliphatic
18 chain or aromatic ring will promote association and phase
19 separation of these groups with development in the
20 product material of toughness and strength. This will be
21 especially the case where an aromatic diisocyanate has
22 been utilised in stage one.

23

24 Figure 1 shows a diagram of a typical end group which
25 could be envisaged as associating in stacks, as shown.
26 The association of many such end groups should provide
27 increased cohesion and strength to the product.

28

29 Once the initial homogeneous mixing has been completed,
30 then the still fluid mix may be poured into suitable
31 containers, such as polypropylene moulds. The
32 polymerisation (curing) of the finished product can then
33 be completed. In order to provide an oxidation resistant

1 product, it is particularly useful to incorporate a
2 reactive antioxidant containing two or more hydroxyl
3 groups, for example, ascorbic acid (alternatively an
4 external anti-oxidants may be used). Alternatively the
5 antioxidant may be added in earlier during the first
6 stage.

7
8 The final product can then be moulded into contact
9 lenses. The product has a number of benefits, in
10 particular as there will be no unreacted extractable
11 groups left in the completed product, it is particularly
12 useful for contact lenses as it is bio-compatible. There
13 is also the benefit that materials made from the final
14 hydrogel product which are soft and strong would be
15 comfortable and re-useable again something which is
16 particularly useful in contact lens manufacture. The
17 final product would also have the benefit of being
18 intrinsically rubbery in their dry state, and therefore
19 contact lenses would not set rigid when dried out. Also,
20 coloured dyes can be put into the final product easily,
21 which cannot be done with similar cross-linked hydrogels
22 and this could be useful when making "fashion" contact
23 lenses, or sun protective or prosthetic contact lenses
24 which have colours, designs or dyes with particular
25 characteristics incorporated into them.

26
27 It can be seen that the embodiments disclosed are both or
28 merely exemplary of the present invention, which may be
29 embodied in many different forms. Therefore, details
30 disclosed herein are not to be interpreted as limiting,
31 but merely as a basis for the claims and for teaching one
32 skilled in art as to the various uses of the present
33 invention in any appropriate matter. In particular, it

1 should be noted that a wide variety of changes can be
2 made in this process.

3
4 For example, pre-polymers with excess OH can be capped
5 with a mono-isocyanate ended aromatic or aliphatic
6 molecule or with a reaction product of a mono-amine with
7 di or higher isocyanate. The low molecular weight amine
8 could be replaced with a low molecular weight polymeric
9 amine, such as low M_n primary and secondary amine ended
10 nylon polyamide) or polypropylene oxide, poly(butanediol)
11 or low molecular weight polymers producing glassy domains
12 such as end-capped polystyrenes or amine end-capped
13 hydrophobic and crystalline domain forms such as
14 poly(ethylene) units. The reaction can be between such
15 amine ended PEGs and PPGs and di or higher amines and di
16 or higher isocyanates, but done in solvents to allow
17 suitable reduced viscosity to be obtained. Also, to slow
18 down the amine reaction, the amine can be added at the
19 outset as the carbonate version of amine carbonate,
20 resulting from the reaction of amine and carbon dioxide.

21
22 Also, stage one hydroxlic excess polymers could be
23 reacted with a phase separating polymer end capped with
24 an anhydride group.

25
26 Finally, it should be noted that this end capping process
27 could be applied to a wide variety of polymers, such as
28 polyesters, nylons, polyurethanes, polyureas, polyethers,
29 polyolefins, polyvinyls and poly(meth)acrylates.

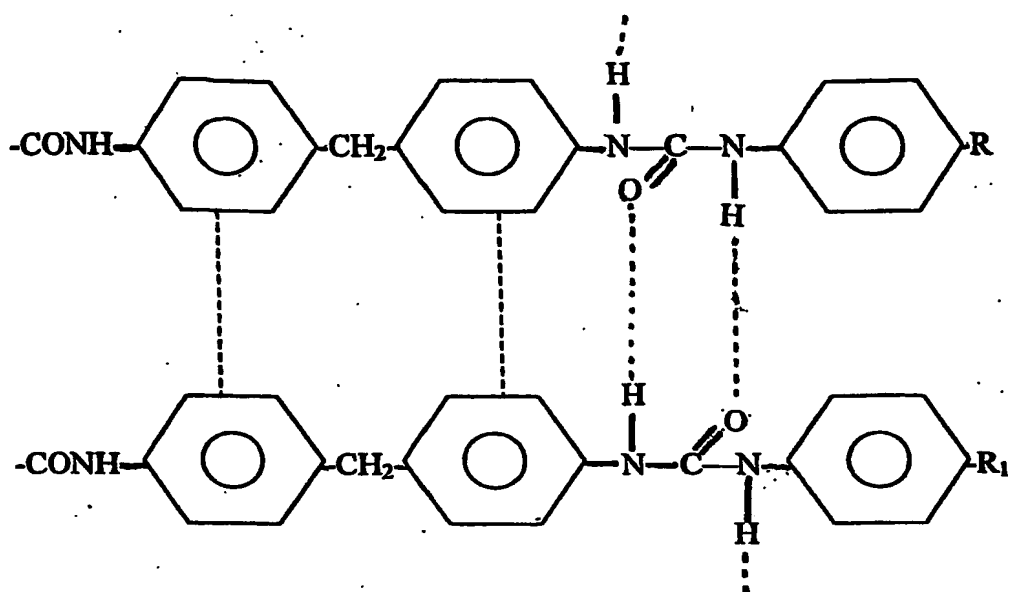


Fig 1

PCT Application
GB0303802



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